Notice of Allowability	Application No.	Applicant(s)	
	10/733,816	HARRISON ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *9/18/2006*.

2. ☒ The allowed claim(s) is/are *27,29-32,34 and 35*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 12/2/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☒ Other *alignments*.

DETAILED ACTION

Status of the Application

Claims 27-36 are pending.

Applicant's election of Group IV, claim 8, drawn to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 in a communication filed on 7/17/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon review of the record, the Examiner contacted Ms Jane Potter to indicate that the elected invention was fully examined in parent application 10/689461 and provided an opportunity to elect a different invention prior examination on the merits. On 9/18/2006, Applicant filed a preliminary amendment canceling claims 1-26 and adding new claims 27-36, which are directed to a method of use of the polypeptide of SEQ ID NO: 2. As indicated by Applicant in the response of 9/18/2006, new claims 27-36 find support in the specification, pages 7-8 and Examples 3-5.

In a telephone conversation with Ms Jane Potter on 10/5/2006, an agreement was reached to amend the specification to correct minor errors, to amend claims 27, 29-30, 32 and 34, and to cancel claims 28, 33 and 36 to place the application in condition for allowance.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/221,242 filed on 07/27/2000.

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 10/211,412 filed on 07/31/2002, and 09/916,109 filed on 07/25/2001.

3. The polypeptide of SEQ ID NO: 2 appears to have been first disclosed in provisional application No. 60/221,242 (shown in Figure 2). The method of claims 27-36 was also first disclosed in this provisional application (pages 7-9; Examples 3-5).

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 12/2/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

5. The drawings submitted on 12/10/2003 have been reviewed and are accepted by the Examiner.

Examiner's Amendment

6. An informal Examiner's amendment to the specification appears below. This amendment merely updates the status of related applications as shown in the first paragraph of the specification.

7. Please enter the following amendments to the specification as follows:

8. On page 1, please replace lines 4-8 as follows:

This application is a divisional application of U.S. Patent Application No. 10/211,412 filed July 31, 2002, now U.S. Patent No. 6716624, which is a divisional application of U.S. Patent Application No. 09/916,109 filed July 25, 2001, now U.S. Patent No. 6465231, which claims the benefit of U.S. Provisional Patent Application No. 60/221,242 filed July 27, 2000, where this provisional application is incorporated herein by reference in its entirety.

9. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

10. Amendments to the specification are required to comply with sequence rules and to correct an obvious error in the sequence identifier used.

11. Authorization for this Examiner's amendment was given in a telephone interview with Ms Jane Potter on 10/5/2006.

12. Please enter the following amendments to the specification as follows:

a. On page 9, line 11, please replace " SEQ ID NO: 8" with " SEQ ID NO: 11".

b. On page 14, line 9, please replace "(EYMPTD)" with "(EYMPTD)(SEQ ID NO: 10)".

13. Please cancel claims 28, 33 and 36.

14. Please replace claims 27, 29-30, 32 and 34 as follows:

27. A method of identifying an inhibitor of GSK3-β, comprising exposing a GSK3-β molecule to a putative inhibitor, and measuring the specific enzymatic activity of said GSK3-β molecule, wherein a reduction in specific enzymatic activity compared to the specific enzymatic activity in the absence of the putative inhibitor indicates that said putative inhibitor is an inhibitor of GSK3-β, and wherein said GSK3-β molecule consists of the amino acid sequence of SEQ ID NO: 2.

29. The method of claim 27, wherein said specific enzymatic activity is Tau protein phosphorylation.

30. The method of claim 29, wherein Tau protein phosphorylation is measured by:

(a) transfecting a cell line with a polynucleotide encoding a Tau protein and a polynucleotide encoding the GSK3-β molecule; and

(b) assaying the phosphorylation of the Tau protein using a monoclonal antibody.

32. The method of claim 29, wherein said Tau protein phosphorylation is measured in a cell-free system by ELISA.

34. A method of identifying an inhibitor of GSK3-β, comprising exposing a GSK3-β molecule to a putative inhibitor attached to a fluorophore, and measuring the fluorescence polarization, wherein the presence of polarization indicates binding of said putative inhibitor to the binding site of GSK3-β, and wherein said GSK3-β molecule consists of SEQ ID NO: 2.

Reasons for Allowance

15. The following is an Examiner's statement of reasons for allowance. Although the prior art discloses a human glycogen synthase kinase 3β, the Examiner has found no teaching or suggestion in the prior art directed to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 (394 amino acids long). The closest homolog to the polypeptide of SEQ ID NO: 2 is the human glycogen synthase kinase 3β (GSK-3β) taught by Stambolic et al. (PIR accession number S53324; EMBL/GenBank accession number P49841, October 1, 1996; cited in the IDS; see attached alignment). The polypeptide of Stambolic et al. (420 amino acids long) has 97.2% sequence identity to the polypeptide of SEQ ID NO: 2 (97.5% = 384x100/394). The polypeptide of SEQ ID NO: 2 comprises amino acids 1-384 of the polypeptide of Stambolic et al. Therefore, claims 27, 29-32, 34-35 directed to a method of identifying

inhibitors of the enzymatic activity of the polypeptide of SEQ ID NO: 2, are allowable over the prior art of record.

Art of Interest

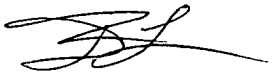
16. Bax et al. (Structure 9:1143-1152, December 2001) discloses a truncated version of human GSK-3β which consists of amino acids 27-393 of the human GSK-3β (420 amino acids long; PIR accession number S53324; EMBL/GenBank accession number P49841) and a histidine tag (page 1145, left column, Results, last complete paragraph).

Conclusion

17. Claims 27, 29-32, 34-35 are allowed.

18. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
November 11, 2006

14	1258	60.5	472	1	T01236	serine/threonine-s
15	1256	60.4	412	1	S37642	protein kinase MSK
16	1249	60.0	403	2	T03777	probable shaggy-li
17	1249	60.0	431	2	S51106	shaggy protein kin
18	1247.5	59.9	469	1	T02256	shaggy protein kin
19	1246	59.9	409	1	S41597	protein kinase ASK
20	1245	59.8	412	2	S71266	shaggy-like protei
21	1244	59.8	411	1	S37643	protein kinase MSK
22	1239	59.5	409	2	S52095	tau-protein kinase
23	1234	59.3	380	2	T04863	shaggy-like protei
24	1233	59.3	412	2	A84715	probable shaggy-li
25	1232	59.2	405	1	S41596	protein kinase ASK
26	1232	59.2	407	2	S77922	shaggy-like protei
27	1229.5	59.1	420	2	A96613	probable glycogen
28	1229.5	59.1	469	1	T02254	shaggy protein kin
29	1228.5	59.0	447	2	F86232	hypothetical prote
30	1226	58.9	411	1	S37644	protein kinase MSK
31	1226	58.9	468	2	T08139	shaggy-like protei
32	1220	58.6	421	2	S51938	protein kinase AtK
33	1208	58.0	447	2	T01756	hypothetical prote
34	1178	56.6	468	2	A55476	protein kinase (EC
35	1158	55.6	431	2	T47908	shaggy-like kinase
36	1156.5	55.6	387	2	T37758	protein kinase skp
37	1109.5	53.3	354	2	T45138	protein kinase skp
38	996	47.9	381	2	T40746	serine-threonine p
39	996	47.9	390	2	T43008	probable protein k
40	978.5	47.0	452	2	T18457	glycogen synthase
41	940.5	45.2	354	2	F90121	hypothetical prote
42	940	45.2	370	2	A56347	protein kinase RIM
43	873.5	42.0	501	2	S67615	MRK1 protein - yea
44	792	38.1	211	2	T04119	probable serine/th
45	735.5	35.3	367	2	T19937	hypothetical prote

ALIGNMENTS

RESULT 1
S53324
glycogen synthase kinase 3 beta (EC 2.7.1.-) - human
C;Species: Homo sapiens (man)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 09-Jul-2004
C;Accession: S53324
R;Stambolic, V.; Woodgett, J.R.
Biochem. J. 303, 701-704, 1994
A;Title: Mitogen inactivation of glycogen synthase kinase-3-beta in intact cells via serine 9 phosphorylation.
A;Reference number: S53324; MUID:95071278; PMID:7980435
A;Accession: S53324
A;Status: preliminary; nucleic acid sequence not shown; translation not shown
A;Molecule type: mRNA
A;Residues: 1-420 <STA>
A;Cross-references: UNIPROT:P49841; UNIPARC:UPI000004E93D; EMBL:L33801; NID:g529236; PIDN:AAA66475.1; PID:g529237
A;Note: the nucleotide sequence was submitted to the EMBL Data Library, August 1994
C;Comment: This enzyme is inhibited by phosphorylation of serine 9 by p70 S6 kinase (see PIR:A41687) or p90 S6 kinase RSK1 (see PIR:I51901).
C;Genetics:
A;Gene: GDB:GSK3B
A;Cross-references: GDB:6108057
C;Superfamily: kinase-related transforming protein; protein kinase homology
C;Keywords: ATP; phosphoprotein; phosphotransferase
F;54-315/Domain: protein kinase homology <KIN>
F;62-70/Region: protein kinase ATP-binding motif
F;9/Binding site: phosphate (Ser) (covalent) (by ribosomal protein S6 kinase) #status experimental
F;85/Active site: Lys #status predicted

Query Match 97.3%; Score 2024; DB 1; Length 420;
Best Local Similarity 100.0%; Pred. No. 2.6e-89;
Matches 384; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy         11 MSGRPRTTSFAESCKPVQQPSAFGSMKVSRDKDGSKVTTVVATPGQGPDRPQEVSYTDTK 70
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSGRPRTTSFAESCKPVQQPSAFGSMKVSRDKDGSKVTTVVATPGQGPDRPQEVSYTDTK 60

Qy         71 VIGNGSFGVVYQAKLCDSGELVAIKKVLQDKRFKNRELQIMRKLDHCNIVRLRYFFYSSG 130
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 VIGNGSFGVVYQAKLCDSGELVAIKKVLQDKRFKNRELQIMRKLDHCNIVRLRYFFYSSG 120

Qy        131 EKKDEVYLNLVLDYVPETVYRVARHYSRAKQTLPVIYVKLYMYQLFRSLAYIHSFGICHR 190
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 EKKDEVYLNLVLDYVPETVYRVARHYSRAKQTLPVIYVKLYMYQLFRSLAYIHSFGICHR 180

Qy        191 DIKPQNLLLDPDTAVLKLCDFGSAKQLVRGEPNVSYICSRYYRAPELIFGATDYTSSIDV 250
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 DIKPQNLLLDPDTAVLKLCDFGSAKQLVRGEPNVSYICSRYYRAPELIFGATDYTSSIDV 240

Qy        251 WSAGCVLAELLLGQPIFPGDSGVDQLVEIIKVLGTPTREQIREMNPNYTEFKFPQIKAHP 310
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 WSAGCVLAELLLGQPIFPGDSGVDQLVEIIKVLGTPTREQIREMNPNYTEFKFPQIKAHP 300

Qy        311 WTKVFRPRTPPEAIALCSRLLEYTPTARLTPLEACAHSFFDELRDPNVKHPNGRDTPALF 370
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 WTKVFRPRTPPEAIALCSRLLEYTPTARLTPLEACAHSFFDELRDPNVKHPNGRDTPALF 360

Qy        371 NFTTQELSSNPPLATILIPPHARI 394
              ||||||||||||||||||||||||
Db        361 NFTTQELSSNPPLATILIPPHARI 384
```

RESULT 2
TVRTKB
tau-protein kinase (EC 2.7.1.135) I - rat
N;Alternate names: factor A; glycogen synthase kinase 3 beta; protein kinase GSK-3-beta; tau-protein kinase I
C;Species: Rattus norvegicus (Norway rat)
C;Date: 31-Dec-1991 #sequence_revision 31-Dec-1991 #text_change 09-Jul-2004
C;Accession: S14708; S33741; S36729
R;Woodgett, J.R.
EMBO J. 9, 2431-2438, 1990